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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,503	03/02/2004	Robert K. Evans	20634YCA	1892

210 7590 11/16/2006

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EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,503	EVANS ET AL.	
	Examiner	Art Unit	
	Benjamin P. Blumel	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-19,21,23-34 and 46-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-19, 21, 23-34, and 46-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2/2004 and 10/6/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the A165 Adenovirus formulation in the reply filed on October 6, 2006 is acknowledged.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on March 2, 2004 and October 6, 2006 were filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

\Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10-18, 21, 24-32, 46-52, 55-60 and 62-67 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 10 and 14 of copending Application No. 11/071,095. Although the conflicting claims are not identical,

they are not patentably distinct from each other because they claim the same invention, therefore the instant invention of the above claims is anticipated.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-18, 21, 24-32, 46-52 and 55-60, 62-67 are rejected under 35 U.S.C. 102(e) as being anticipated by Wu et al., (US 2002/0031527).

The instant invention is drawn to an adenovirus formulation, which comprises a purified virus, a buffer, a sugar, a salt, a divalent cation, a non-ionic detergent and at least one free radical oxidation inhibitor with an osmolarity of 200mOs/L to 800mOs/L. The purified virus ranges from 10^7 to 10^{13} vp/ml, the buffer is Tris at 1-10mM and a pH of 7.5-8.5, the salt is NaCl at 75mM, the divalent cation is $MgCl_2$ at a molarity of 1mM, the non-ionic detergent is Polysorbate-80 (Tween-80) at 0.02%, the free radical oxidation inhibitors are histidine at 10mM, EDTA at 100uM and ethanol at 0.5%.

Wu et al. teach the formulation of Adenovirus for gene therapy. The goal of their work was to develop liquid and lyophilized adenovirus formulations, which remain infective after incubating at 4°C for 6 months. The formulations taught by Wu et al. contain Adenovirus

formulations with titers of 10^9 pfu/ml that contain sucrose, Tween-80, NaCl, $MgCl_2$, histidine, mono-Tris and the use of antioxidants to inhibit oxidation. The amounts of each component used are sucrose at 2.5-10%, mono-Tris or histidine at 1mM-50mM and a pH of 8.2, 1mM of $MgCl_2$, Tween-80 at 0.02-5%, and 150mM of NaCl. These components were used in multiple arrangements in order to optimize for the most stable formulation. Wu et al. do not specifically teach the use of EDTA or Ethanol, but they do teach that any known antioxidants (such as EDTA and Ethanol) can be used to inhibit oxidation. In light of the teachings from Evans et al., (Journal of Pharmaceutical Sciences, 2000), this combination would be ideal in the formulations of Wu et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-19, 21, 23-34, 46-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. in view of Evans et al., (Journal of Pharmaceutical Sciences, 2000) and Binley et al., (US 6,710,173 B1).

The instant invention as stated above is also drawn to an adenovirus formulation also comprising DNA plasmid at a concentration of 1 mg/ml. In addition, the applicants have elected the adenovirus formulation A165.

Wu et al. as discussed above disclose the development of stable adenovirus formulations. Even though Wu et al. do not teach the exact amounts of each component for the specific

formulation elected, optimization of the formulations is critical for determining the most stable composition for each environmental condition. Therefore, the teachings of Wu et al. would provide the information necessary to arrive at various formulations which may include that of A165. However, Wu et al. do not disclose DNA plasmids being present at any concentration or the specific oxidation inhibitors of ethanol and EDTA.

Binley et al. teach that vaccine combinations comprising replication competent viral vector and DNA plasmids are possible vaccine compositions. *See column 6, lines 47-51.*

Evans et al. teach the beneficial application of a EDTA/Ethanol mixture towards improving DNA stability. Evans et al. investigated what effect EDTA at 0.5mM and Ethanol at 1% might had on supercoiled DNA, separately and combined. The combination had an additive effect towards increasing the DNA stability of the supercoiled DNA while the EDTA or Ethanol alone did not.

It would have been obvious to one of ordinary skill in the art to modify the formulations taught by Wu et al. in order to provide a adenovirus formulation according to the instant invention. One would have been motivated to do so, given the suggestion by Binley et al. that the vaccines compositions can have replication competent viral vectors and DNA plasmids together in addition to other immunogenic components. There would have been a reasonable expectation of success, given the knowledge that vaccine combinations of viruses and DNA plasmids are possible vaccine compositions, as taught by Brinley et al., and also given the knowledge that the combination of Ethanol and EDTA stabilizes DNA, as taught by Evans et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin P. Blumel whose telephone number is 571-272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Benjamin Blumel
Patent Examiner

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